REMARKS

Claims 1-72 were pending prior to this Response, with claims 1-64 being withdrawn in response to a restriction requirement. By the present communication, no claims have been added, claims 1-64 and 72 have been cancelled without prejudice, and claim 56 has been amended to recite Applicants' invention with greater particularity. The amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 65-71 are currently pending in this application.

The Information Disclosure Statement

The Office Action alleges that the Information Disclosure Statement filed May 19, 2003 (Paper No. 8) fails to comply with the provisions of MPEP § 609 for various reasons. However, Applicants respectfully submit that the present application was filed under the provisions of 37 CFR 1.53(b). MPEP § 609 (I)(A)(2) provides (in part) as follows:

> The examiner will consider information which has been considered by the Office in a parent application when examining . . . (C) a continuation-in-part application filed under 37 CFR 1.53(b). Such information need not be resubmitted in the continuing application unless the applicant desires the information to be printed on the patent.

Therefore, Applicants respectfully request that the Examiner consider in this application all art considered in the parent applications identified in the priority claim for this application in the Corrected Filing Receipt mailed April 14, 2003, in accordance with the provisions of MPEP § 609 (I)(A)(2). To assure that the information is printed on the face of the patent, Applicants submit herewith an Information Disclosure Statement listing all references cited in the priority documents on PTO Form 1449. Additional copies of the references are not provided since they are available in the priority applications.

The Rejection under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection under 35 U.S.C. § 112, first paragraph, of claims 65-71 as containing subject matter that was not sufficiently described in the specification as to reasonably convey to those skilled in the art that Applicants were in possession of the invention as claimed. In particular, Applicants disagree with the Examiner's assertion: "the disclosure fails to describe the common attributes that can link together all of the microenvironments, clones, probes and markers that should be screened and thus included in this enormous genus from the few examples provided by the applicants" (Office Action, page 8).

However, Applicants respectfully submit that the analogy used by the Examiner comparing a method claim to a chemical compound (i.e., what atoms are included) is not apt. In these method claims, the framework that links together the terms in the claims is the syntax of English and the methodology (series of acts) of the claim in which the terms appear. Moreover, Applicants submit that the Specification gives more than one, and in some cases a plethora, of specific examples illustrating the very terms identified by the Examiner as lacking requisite specificity to support the broad terms in the claims.

As examples of "microenvironments" the Specification recites gel microdroplets (GMDs), beads, and a variety of liposomes (Specification, page 23, line 15 to page 25, , line 7). The term "microenvironments" is specifically defined as "any molecular structure which provides an appropriate environment for facilitating the interactions necessary for the method of the invention" (Specification, page 24, lines 27-29). Accordingly, by the present response, claim 56 has been amended to recite "a microenvironment suitable for growth of the organisms". Therefore, Applicants submit that those of skill in the art would have understood that Applicants had possession of the scope of the term "microenvironment" at the filing of the application.

With regard to the term "mixed population of organisms" the examples provided are indeed numerous: "insect feces, soil, water, *etc*"; "an extract from blood, urine, spinal fluid, tissue, vaginal swab, stool, amniotic fluid or buccal mouthwash" from any mammalian organism. For non-mammalian (*e.g.*, invertebrates) organisms the specific examples of mixed populations of organisms are "tissue samples, salivary samples, fecal material or material in the digestive tract of the organism". Such mixed populations of organisms are described as available in specific locations known to those of skill in the art, such as "hot sulfur pools, volcanic vents, and frozen tundra" in "plants, fertilizer, soil, liquid or other horticultural or agricultural product"; in "infant formula, seafood, fresh produce and packaged food"; in "soil, sewage treatment sludge" and in "blood, soil and sludge" (two paragraphs beginning at page 34, line 13). Specific examples of "markers" described in the Specification are those "selected on the basis of detection of radioactivity, enzymatic activity; fluorescence, of any optical feature, of a magnetic property (e.g., using magnetic beads), of immunoreactivity, and of hybridization" (page 74, paragraph beginning at line 5. The background recites numerous fluorescent markers used in flow cytometry, including "a range of fluorogenic esters including fluorescein diacetate (FDA) derivatives and CemChrome B" (page 9, lines 13-18).

In view of the extensive listing of "representative examples" of the terms used in the claims, Applicants submit that those of skill in the art would understand that the Applicants were "in possession" of the invention as claimed and would have understood their intention at filing of the application that the invention could be practiced in accordance with the full scope of claim 56, rather than being limited to the particular example(s) used to illustrate the invention in the Examples of the Specification.

Accordingly, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 112, first paragraph, for allegedly lacking sufficient written description to support the claims are respectfully requested.

The Rejection under 35 U.S.C. § 102(b)

A. Applicants respectfully traverse the rejection of claims 65-67 under 35 U.S.C. § 102(b) as allegedly being anticipated by Powell et al. (*Biotechnology*, (April 1990) 8,4:333-337. However, Applicants respectfully submit that the invention methods for obtaining an organism from a mixed population of organisms in a sample, as defined by amended claim 65 (and claims 66-67), distinguish over the disclosure of Powell et al. by requiring:

"encapsulating two or more organisms obtained from the sample, each in a microenvironment growth of the organisms;

incubating the encapsulated two or more organisms under such conditions and for such a time to allow the two or more organisms to grow; and

sorting the microenvironments by a flow cytometer on the basis of growth of the organism to obtain an organism from the sample that grows under the conditions." It should be noted that Applicants' claims do not require secretion or production of any analyte as the basis of cell separation.

By contrast, Powell et al. fail to disclose encapsulating organisms within a microenvironment, incubating the organisms and then sorting the encapsulated organisms using a flow cytometer to separate cells on the basis of growth of the organisms, i.e., to separate organisms that grow under the incubation conditions from cells that do not grow under the incubation conditions. In fact, Applicants submit that Powell et al. are concerned with using gel microdroplets and flow cytometry, not as an assay for organism growth, but to determine a product secreted from an organism, which product becomes the analyte. Thus Weaver et al. fail to disclose at least two elements of claims 65-69.

Anticipation under 35 U.S.C. § 102(b) requires that the reference recite each and every element of the claims in a single document. Since Powell et al. fails to disclose each and every element of the invention methods, as defined by amended claim 65, Applicants respectfully submit that the Examiner has failed to establish anticipation under 35 U.S.C. § 102 (b) over Powell et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully presented.

B. Applicants also respectfully traverse the rejection of claims 65-69 under 35 U.S.C. § 102(b) as allegedly being anticipated by Weaver et al. (U.S. Patent No. 5,055,390). Applicants respectfully submit that the invention methods for obtaining an organism from a mixed population of organisms in a sample, as defined by amended claim 65 (and claims 66-69), distinguish over the disclosure of Weaver et al. by requiring:

"encapsulating two or more organisms obtained from the sample, each in a microenvironment suitable for growth of the organisms;

incubating the encapsulated two or more organisms under such conditions and for such a time to allow the two or more organisms to grow; and

sorting the microenvironments by a flow cytometer on the basis of growth of the organism to obtain an organism from the sample that grows under the conditions." It should be noted that Applicants' claims do not require secretion or production of any analyte as the basis of cell separation.

By contrast, Weaver et al. disclose methods for fusing the contents of microdroplets in *a non-aqueous environment* to accomplish chemical manipulation of contents of microdroplets by introducing substances, such as tracers (Col. 27, lines 8-50) into one set of the microdroplets. In general, non-aqueous environments are not suitable for growing organisms. Alternatively, Weaver et al. disclose only capturing of molecules

at binding sites in gel microdroplets, such as molecules that are released from biological entities within the microdroplets. When Weaver considers incubation of "entities" within the microdroplets, it is for the purpose of allowing the entities "to produce and secrete molecules . . . thereby resulting in capture of more molecules at binding sites within such GMDs" (Col. 29, lines 25-33). Thus, Weaver et al. fail to disclose encapsulating organisms within a microenvironment suitable for organism growth, incubating the organisms under conditions suitable for such growth, and then sorting the encapsulated organisms using a flow cytometer to separate microenvironments on the basis of growth of the organisms, i.e., to separate organisms that grow under the incubation conditions from organisms that do not grow under the incubation conditions. In addition, Weaver fails to disclose any method for screening organisms for growth without relying on fusion of microdroplets in a non-aqueous environment as described by Weaver or detection of secreted products. Thus Weaver et al. fail to disclose each and every element of claims 65-69.

Anticipation under 35 U.S.C. § 102(b) requires that the reference recite each and every element of the claims in a single document. Since Weaver et al. fails to disclose each and every element of the invention methods, as defined by amended claim 65, Applicants respectfully submit that the Examiner has failed to establish anticipation under 35 U.S.C. § 102 (b) over Weaver et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully presented.

C. Applicants also respectfully traverse the rejection of claims 65-70 under 35 U.S.C. § 102(b) as allegedly being anticipated by Thompson et al. (U.S. Patent No. 5,824,485). Applicants respectfully submit that the invention methods for obtaining an organism from a mixed population of organisms in a sample, as defined by amended claim 65 (and claims 66-70), distinguish over the disclosure of Thompson et al. by requiring:

"encapsulating two or more organisms obtained from the sample, each in a microenvironment suitable for organism growth;

incubating the encapsulated two or more organisms under such conditions and for such a time to allow the two or more organisms to grow; and

sorting the microenvironments by a flow cytometer on the basis of growth of the organism to obtain an organism from the sample that grows under the conditions."

By contrast, Thompson et al. fail to disclose sorting gel microdroplets by a flow cytometer to obtain a native organism from the sample on the basis of growth of the organism, i.e., to separate organisms that grow under the incubation conditions from those that do not grow under the incubation conditions. In fact, Applicants submit that Thompson et al. describe screening "combinatorial gene libraries" in host organisms to determine a product secreted from a host organism. Thus, as the Examiner acknowledges (Office Action, page 13), Thompson speaks of native organisms from environmental samples as "donor organisms useful for preparing a combinatorial gene expression library."

Applicants submit that Thompson et al are absolutely silent regarding use of gel microdroplets (or any other type of microenvironment) and flow cytometry as a means of sorting native organisms to distinguish between those that have grown during incubation *in vitro* from those that have not. Thus Thompson et al. fail to disclose each an every element of claims 65-69.

Anticipation under 35 U.S.C. § 102(b) requires that the reference recite each and every element of the claims in a single document. Since Thompson et al. fail to disclose each and every element of the invention methods, as defined by amended clam 65, Applicants respectfully submit that the Examiner has failed to establish anticipation

under 35 U.S.C. § 102 (b) over Weaver et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully presented.

The Rejection Under 35 U.S.C. § 103(a)

Applicants respectfully traverse the rejection of claims 65-71 under 35 U.S.C. § 103(a) as being unpatentable over the combined disclosures of Thompson et al. (U.S. Patent No. 5,824,485) and Kotitz et al. Applicants' remarks above regarding the failure of Thompson to disclose the invention methods apply equally and are incorporated here. In addition, Applicants submit that Thompson et al. fail to suggest the invention methods, as defined by claim 65, or claims 70-71, because Thompson et al. describe construction of libraries of host organisms that are "engineered" to contain one or more sequences from one or more "donor" organisms, including, among others, physiological probes and "chemoresponsive promoters to modulate transcription of a reporter gene only in the presence of a certain kind of activity or a certain class of compounds" (Col. 35, lines 40-56). Applicants submit that Thompson's very emphasis upon chimeric engineered libraries and screening of transfected host cells on the basis of whether the organism secretes a product or interacts in some way with an introduced sequence would lead those of skill in the art away from the simplicity of screening encapsulated native organisms using flow cytometry on the basis of growth of the organism (whether assisted by a magnetic field sensing device or not). Thus, Applicants submit that Thompson et al do not themselves suggest modification of the reference along the lines of Applicants' invention. Moreover, even if those of skill in the art were motivated by Thompson to modify Thompson's disclosure to arrive at the invention methods, there would be no reasonable expectation of success, especially with respect to organisms obtained from environmental samples. As Applicants teach in the Background of the Specification, most of such organisms have not been successfully cultured in vitro, thus providing those of skill in the art with doubt that a method along the lines of the invention could or would succeed.

Furthermore, Applicants submit that the deficiencies of Thompson for disclosing or suggesting the invention methods, as defined by presently presented claims 65-71, are not overcome by Kotitz et al. Although Kotitz et al. disclose use of SQUID-based magnetic nanoparticle relaxation measures as a tool for quantitative determination of biological *binding reactions*, Kotitz et al. are silent regarding use of SQUID or any other type of magnetic field sensing device for flow cytometry screening to distinguish between microenvironments, such as gel microdroplets, containing organisms that have grown during incubation in a microenvironment and those containing organisms that did not grow under such conditions.

Thus Applicants submit that *prima facie* obviousness of the invention over Thompson et al. and Kotitz et al., either alone or in combination has not been shown by the Examiner. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 for alleged lack of patentability are respectfully requested.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 56-71 clearly and patentably define the invention and respectfully request that the Examiner withdraw all rejections and pass the application to allowance. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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